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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,029	04/16/2007	Hyung Ook Kim	930086-2032	6043

7590 12/11/2008

RONALD R. SANTUCCI, ESQ
C/O FROMMER LAWRENCE & HAUG LLP
745 FIFTH AVENUE
NEW YORK, NY 10151

EXAMINER	
RAHMANI, NILOOFAR	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
12/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,029	KIM ET AL.	
	Examiner	Art Unit	
	NILOOFAR RAHMANI	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6,11 and 12* is/are allowed.

6)☒ Claim(s) *1,3,5 and 13-21* is/are rejected.

7)☒ Claim(s) *2,4 and 7-10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/15/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-21 are currently pending in the instant application.

Priority

2. This application was filed on 04/16/2007, and is a 371 of PCT/KR04/03545, filed on 12/30/2004, and claims priority of REPUBLIC OF KOREA 10-2003-0100132, filed on 12/30/2003.

The claimed benefit of priority date is denied. There is no certified translation of the priority document. The filing date of the instant application is 12/30/2004.

3. *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is rejected because the term " alkylester compound containing R6" is confusing. What is "alkylester compound containing R6"? Correction is required.

4. Claim 5 is rejected because the term " metal reagent containing R7" is confusing. What is "metal reagent containing R7"? Correction is required.

5. Claims 15, 17-18, 20 are rejected because the term " therapeutic agent' is confusing. Are they claiming "pharmaceutical composition"? Correction is required.

6. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition TNF-α receptor, does not reasonably provide enablement for treat and prevent any and all diseases mediated by this receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the

disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims.
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to a therapeutic agent comprising of formula (I) or its pharmaceutically acceptable salt effective in treating inflammatory disease, immune-related diseases.

The state of the prior art: " At the time that the invention was made, the scientific literature tends to show the speculative role of the TNF-α receptor and its role in the treatment of inflammatory diseases. "Although sTNFR:Ig protein can be induced by either TNF-alpha or interleukin (IL)-1beta, its antagonist activity is limited to the former cytokine. The SAA2-tat/HIV-sTNFR:Ig construct, and derivatives thereof, may therefore be ideally suited to gene therapy applications that require the local production of potent and specific immune modifiers only when there is active pathology. It may consequently be of particular use in the future treatment of diseases such as rheumatoid arthritis." (Emphasis added). Rygg M et al., Scandinavian journal of immunology, (2001 Jun), Vol. 53, No. 6, pp. 588-95.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be useful for treating a pharmacological condition in a subject.

Amount of guidance/working examples: Applicant provides examples of the test compounds to inhibit TNF-α on Tables 1-7, pages 91-104. However, There is no guidance for using a therapeutically effective amount of a compound of Formula (I) could treat any and all TNF-α related disease. Nor does applicant identify what diseases are treatable by therapeutically effective amount of a compound of Formula (I).

The breadth of the claims: The breadth of claims is drawn to a therapeutic agent comprising of formula (I) or its pharmaceutically acceptable salt effective in treating inflammatory disease, immune-related diseases.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 13-21, for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, have been enabled by the instant specification.

7. *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* ***v.*** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

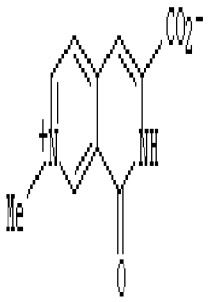
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 103(a) as being unpatentable over Trommer et al., Tetrahedron Letters (1973), (17), 1447-8.

Determination of the scope and content of the prior art (MPEP §2141.01)

Trommer et al. disclosed analogous compounds, which from the STN search are

RN 42285-32-5
CN 2,7-Naphthyridinium, 6-carboxy-7,8-dihydro-2-methyl-8-oxo-, inner salt



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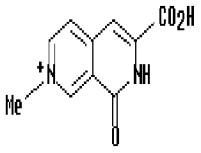
RN 42285-33-6
CN 2,7-Naphthyridinium, 6-carboxy-7,8-dihydro-2-methyl-8-oxo-, chloride (1:1)



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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claim and the prior art compound is that the instant claim replaces one Me of the prior art compound with a Hydrogen.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compounds of Trommer et al. to obtain the instantly claimed compounds.

A compound that differs only in molecular arrangement from the compounds disclosed in the prior art and which for which no unexpected properties of this compound are disclosed in the specification is unpatenable, *Ex parte KRUEGER AND HAYES*, 121 USPQ 420, *In re NORRIS*, 84 USPQ 458, *In re Hass* 60 USPQ 552, which found a *prima facia* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, *Ex parte Ullyot*, 103 USPQ 185, which found a *prima facia* case of obviousness of 2-oxo-quinolines over a 1-oxo-isoquinoline taught in the prior art, *In re FINLEY,* 81 USPQ 383 , which found a *prima facia* case of obviousness of 2-ethyl hexyl salicylate over octyl salicylate taught in the prior art.

Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these

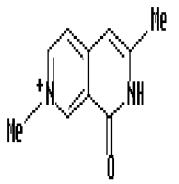
presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

8. Claim 1 is rejected under 103(a) as being unpatentable over Birkofer et al., Chemische Berichte (1957), 90, 2933-40.

Determination of the scope and content of the prior art (MPEP §2141.01)

Birkofer et al. disclosed analogous compounds, which from the STN search are

RN 112689-01-7
CN 2,7-Naphthyridinium, 3,7-dimethyl-1-oxo-, iodide



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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claim and the prior art compound is that the instant claim replaces one Me of the prior art compound with a Hydrogen.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compounds of Birkofer et al. to obtain the instantly claimed compounds.

A compound that differs only in molecular arrangement from the compounds disclosed in the prior art and which for which no unexpected properties of this compound are disclosed in the specification is unpatenable, *Ex parte KRUEGER AND HAYES*, 121 USPQ 420, *In re NORRIS*, 84 USPQ 458, *In re Hass* 60 USPQ 552, which found a *prima facia* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, *Ex parte Ullyot*, 103 USPQ 185, which found a *prima facia* case of obviousness of 2-oxo-quinolines over a 1-oxo-isoquinoline taught in the prior art, *In re FINLEY,* 81 USPQ 383 , which found a *prima facia* case of obviousness of 2-ethyl hexyl salicylate over octyl salicylate taught in the prior art.

Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re*

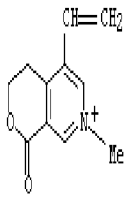
Wiechert, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

9. Claims 1, 3 are rejected under 103(a) as being unpatentable over Govindachari et al., Journal of the Chemical Society (1957) 551-6.

Determination of the scope and content of the prior art (MPEP §2141.01)

Govindachari et al. disclosed analogous compounds, which from the STN search are

RN 117885-38-8
CN 1H-Pyrano[3,4-c]pyridinium, 5-ethenyl-3,4-dihydro-7-methyl-1-oxo-



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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claim and the prior art compound is that the instant claim replaces one Me of the prior art compound with a Hydrogen.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compounds of Govindachari et al. to obtain the instantly claimed compounds.

A compound that differs only in molecular arrangement from the compounds disclosed in the prior art and which for which no unexpected properties of this compound are disclosed in the specification is unpatenable, *Ex*

parte KRUEGER AND HAYES, 121 USPQ 420, *In re NORRIS*, 84 USPQ 458, *In re Hass* 60 USPQ 552, which found a *prima facia* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, *Ex parte Ullyot*, 103 USPQ 185, which found a *prima facia* case of obviousness of 2-oxo-quinolines over a 1-oxo-isoquinoline taught in the prior art, *In re FINLEY,* 81 USPQ 383 , which found a *prima facia* case of obviousness of 2-ethyl hexyl salicylate over octyl salicylate taught in the prior art.

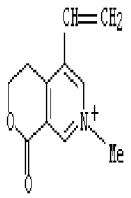
Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

10. Claims 1, 3 are rejected under 103(a) as being unpatentable over Eugster et al., Helvetica Chimica Acta (1957), 40, 69-79.

Determination of the scope and content of the prior art (MPEP §2141.01)

Eugster et al. disclosed analogous compounds, which from the STN search are

RN 117885-38-8
CN 1H-Pyrano[3,4-c]pyridinium, 5-ethenyl-3,4-dihydro-7-methyl-1-oxo-



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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claim and the prior art compound is that the instant claim replaces one Me of the prior art compound with a Hydrogen.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compounds of Eugster et al. to obtain the instantly claimed compounds.

A compound that differs only in molecular arrangement from the compounds disclosed in the prior art and which for which no unexpected properties of this compound are disclosed in the specification is unpatenable, *Ex parte KRUEGER AND HAYES*, 121 USPQ 420, *In re NORRIS*, 84 USPQ 458, *In re Hass* 60 USPQ 552, which found a *prima facia* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, *Ex parte Ullyot*, 103 USPQ 185, which found a *prima facia* case of obviousness of 2-oxo-quinolines over a 1-oxo-isoquinoline taught in the prior art, *In re FINLEY,* 81

USPQ 383 , which found a *prima facia* case of obviousness of 2-ethyl hexyl salicylate over octyl salicylate taught in the prior art.

Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

11. *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

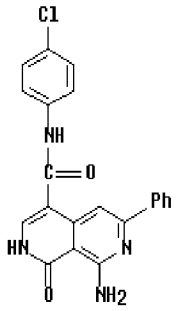
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Elmaati et al., Journal of the Chinese Chemical Society (Taipei,

Taiwan) (2002), 49(6), 1045-1050. Elmaati et al. discloses the instant claimed compound, which from the STN search is

RN 517907-24-3

CN 2,7-Naphthyridine-4-carboxamide, 8-amino-N-(4-chlorophenyl)-1,2-dihydro-1- oxo-6-phenyl-

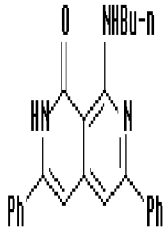


, which anticipates the instant compounds when X is O , Y is N, and R_1 is amino, R_4 is acylamino in the instant application. Therefore, the instant claims are anticipated by Elmaati et al.

12. Claims 1, 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Allan et al., Journal of Heterocyclic Chemistry (1970), 7(3), 495-507. Van Allan et al. discloses the instant claimed compound, which from the STN search is

RN 27337-98-0

CN 2,7-Naphthyridin-1(2H)-one, 8-(butylamino)-3,6-diphenyl-



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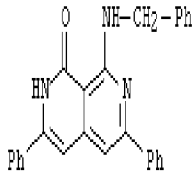
RN 27338-00-7

CN 2,7-Naphthyridin-1(2H)-one, 3,6-diphenyl-8-[(phenylmethyl)amino]-



, which anticipates the instant compounds when X is O , Y is N, and R_1 is C1-C10 alkyl amino, R_6 is aryl in the instant application. Therefore, the instant claims are anticipated by Van Allan et al.

13. ***Claim Objections***

Claims 2, 4, 7-10 are objected to as being dependent upon a cancelled base claims 1, 5, but would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims.

14. ***Allowable Subject Matter***

Claims 6 and 11-12 are patentable over Van Allan et al., Journal of Heterocyclic Chemistry (1970), 7(3), 495-507. The reference teaches different

process to make compound of formula (I). Therefore, the claims are free of prior art.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
/NILOOFAR RAHMANI/

12/03/2008

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625